REMARKS

Claims 1 to 33 are pending in the application. The Applicant has amended Claims 1-33, to particularly point and distinctly claim the subject matter that Applicant regards as his invention. Support for the present amendments is found throughout the specification and claims, as originally filed. No new matter has been added and no additional claims fees are believed to be due. The Applicant strongly believes that the present amendments and below remarks have placed the present application in condition for allowance. Accordingly favorable and timely action are respectfully requested.

Rejection under 35 USC § 112, First Paragraph

The Examiner has rejected Claims 1-33 under 35 USC § 112, first paragraph, as allegedly the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention. Specifically, the Examiner has asserted that present specification does not reasonably provide enablement for the aforementioned claims' recitation of "2-decarboxy-2-phosphinico prostaglandin derivative" or "derivative." The Examiner's attention is respectfully directed to the "Amendments" section of the instant paper, in which the Applicant has amended the aforementioned claims to substitute the term "derivative" with "compound", only to obviate the Examiner's rejection and expedite allowance of the present case. Accordingly, reconsideration and withdrawal of the rejection of Claims 1-33 under 35 USC § 112, first paragraph, are respectfully requested.

Rejection under 35 USC §112, Second Paragraph

The Examiner has rejected Claim 1 under 35 USC § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner asserts that the aforementioned claim's recitation of the terms "biohydrolyzable amide," "biohydrolyzable ester," "biohydrolyzable imide" and "salt" are not clear. To clarify, the Applicant asserts that the phrase "the salt of the structure" is intended to mean that the salt is an addition salt of an acid. Further, the Applicant asserts that the salt is intended to be part of the Markush element. Moreover, the Applicant asserts that the hydrolysable ester is intended to refer to a precursor that may be hydrolyzed into one of the Markush compounds. In light of the above clarification, reconsideration and withdrawal of the rejection to Claim 1 under 35 USC § 112, second paragraph, are respectfully requested.

Rejection under 35 USC § 102(b) over Aristoff

The Examiner has rejected Claims 1-33 under 35 USC § 102(b) as allegedly anticipated by Aristoff et al., AN: 1982:406057 (hereinafter "Aristoff"). Specifically, the Examiner asserts that Aristoff discloses an intermediate species RN 76794-01-9, which purportedly is a species of the first compound in present claim 29, wherein "a" is a double bond. The Examiner's rejection is respectfully traversed.

The Applicant respectfully submits that Aristoff fails to anticipate the compounds of the present invention. Aristoff discloses an intermediate species of phosphonic acid, rather than the phosphinic acid compounds claimed herein. It is clear from the Applicant's definition of the various R group substituents of the compounds claimed herein that it is impossible for the first compound of claim 29 to take the form of a phosphonic acid. To be inclusive of phosphonic derivatives, the R_1 and R_3 substituents of the present compound would both have to be oxygen-containing moieties. On the contrary, the Applicant has explicitly limited the Markush group of R_1 to include only hydrogen atoms, monovalent hydrocarbon groups having 1 to 4 carbon atoms, and monovalent heterogenous groups having 1 to 4 member atoms. Thus, it is clear then that the compounds of claim 29 cannot take the form of phosphonic acid, and therefore, cannot be anticipated by Aristoff's disclosure of a phosphonic intermediate.

The Applicant wishes to underscore to the Examiner the importance of the above distinction between the phosphonic intermediate compound disclosed by Aristoff and the phosphinic compounds claimed herein. Indeed, the phosphonic derivatives obtained from the intermediate compound disclosed by Aristoff have been demonstrated to be substantially inactive, and thus, ineffective in the context of the present invention. Moreover, the Applicant, via his vast research and development of the present invention, has learned that the high acidity of phosphonic compounds discourages their penetration into the lipid-rich membrane of target cells. The Applicant has further and surprisingly discovered that some degree of protonation is required for the administration of the subject prostaglandin into target cells. For this reason, the Applicant focused his research endeavors on the use of a phosphinic compound as a prostaglandin derivative, mainly because of its possession of the moderated level of acidity and partial protonation required for penetration of the membrane of target cells. Thus, the Applicant respectfully submits and strongly urges that the active, phosphinic compounds of the present invention cannot be anticipated by the substantially inactive, phosphonic intermediate compounds disclosed by Aristoff. Reconsideration and withdrawal of the rejection to Claims 1-33 under 35 USC § 102(b) are therefore respectfully requested.

Rejection under 35 USC § 102(b) over Biddlecom

The Examiner has rejected Claims 1-33 under 35 USC § 102(b) as allegedly anticipated by US Patent Number 4,171,331 to Biddlecom et al (hereinafter "Biddlecom"). The Examiner's rejection is respectfully traversed.

The Applicant wishes to note and underscore to the Examiner that the present application lays claim to a phosphinic acid, rather than the phosphonic derivative disclosed by Biddlecom. The differences between these two compounds are quite significant, particularly when considered in light of the fact that the latter, phosphonic derivatives have been demonstrated to be inactive, and thus, ineffective in the context of the present invention. Moreover, the Applicant has learned that the high acidity of phosphonic derivatives discourages their penetration into the lipid-rich membrane of target cells. The

Applicant has further and surprisingly discovered that some degree of protonation is required for the administration of the subject prostaglandin into target cells.

The Applicant respectfully directs the distinguished Examiner's attention to the pending claims. It is clear from the Applicants' definition of the various R group substituents of the compounds claimed therein that it is impossible for the any of the claimed compounds to take the form of a phosphonic acid. To be inclusive of phosphonic derivatives, the R_1 and R_3 substituents of the present compounds would both have to be oxygen-containing moieties. On the contrary, the Applicant has explicitly limited the Markush group of R_1 to include only hydrogen atoms, monovalent hydrocarbon groups having 1 to 4 carbon atoms, and monovalent heterogenous groups having 1 to 4 member atoms. Thus, it is clear then that prostaglandin compounds of the present invention cannot take the form of phosphonic acid, and therefore, cannot be anticipated by Biddlecom's disclosure of a phosphonic derivative. Reconsideration and withdrawal of the rejection to Claims 1-33 under 35 USC § 102(b) are therefore respectfully requested.

Reminder Under 37 CFR § 1.56 Regarding Joint Inventorship

The Applicant duly thanks the Examiner for reminding the Applicant of his obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 USC § 103(c) and potential 35 USC § 102(f) or (g) prior art under 35 USC § 103(a). The Applicant respectfully submits that the entirety of the claims pending in the present application was commonly owned from the time of conception to the present. Further, as the present application only names a single inventor, the above-listed sections of 35 USC § 103 are not applicable in the present context.

Rejection under 35 USC § 103(a) over Biddlecom

The Examiner has rejected Claims 1-33 under 35 USC § 103(a) as allegedly obvious over Biddlecom. The Examiner's rejection is respectfully traversed.

The Applicant again wishes to underscore to the distinguished Examiner that Biddlecom discloses and relates entirely to the substantially inactive compound, phosphonic acid, rather than the active, phosphinic acid prostaglandin derivatives claimed herein. The Examiner's attention is again directed to the pending claims of the instant application. It is clear from a thorough review of said formula that it is impossible for any of the claimed, general structures to be inclusive of phosphonic acid, as inclusion of phosphonic acid would require that the substituents R_1 and R_3 both be oxygen-containing moieties. However, the Applicant has defined the substituent R_1 to include only hydrogen atoms, monovalent hydrocarbon groups having 1 to 4 carbon atoms, and monovalent heterogenous groups having 1 to 4 member atoms. Thus, the compounds of the present invention cannot take the form of phosphonic acid, and therefore, can neither be anticipated nor rendered obvious by Biddlecom's disclosure of a phosphonic derivative.

Further, the Applicant wishes to underscore to the Examiner that, as the preceding section revealed, the Applicant has determined that the phosphonic acid compounds

disclosed by Biddlecom are substantially inactive, and thus, are not suitable for use in the context of the present invention. The Applicant has discovered that the phosphonic acid compound is too acidic to penetrate the lipid-rich membrane of target cells. The Applicant has further and surprisingly discovered that phosphinic acid compounds, possess the moderated level of acidity and partial protonation required for their penetration of the membrane of target cells. Thus, the Applicant submits and strongly urges that it would not have been obvious to a person of ordinary skill in the art, at the time the invention was made, to employ an active, phosphinic acid compound as a prostaglandin derivative for, among other things, the treatment of hair loss, from reviewing Biddlecom's disclosure of an substantially inactive, phosphonic acid compound. Reconsideration and withdrawal of the rejection to Claims 1-33 under 35 USC § 103(a) are therefore respectfully requested.

CONCLUSION

Attached at the conclusion of this communication is a "Version with Markings to Show Changes Made." Applicant has made an earnest effort to place the present claims in condition for allowance. WHEREFORE, entry of the amendments provided herewith, reconsideration of the claims as amended in light of the Remarks provided, withdrawal of the claims rejections, and allowance of Claims 1-33, as amended, are respectfully requested. In the event that issues remain prior to allowance of the noted claims, then the Examiner is invited to call Applicant's undersigned attorney to discuss any remaining issues.

Respectfully submitted,

MITCHELL ANTHONY DELONG

By _____

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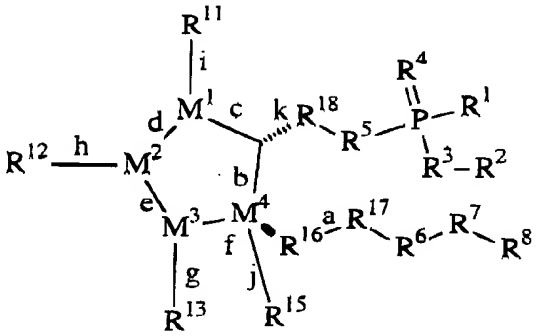
(513) 634-9315

04 October 2002
Cincinnati, Ohio
Case 8191-OA.doc

VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. A 2-decarboxy-2-phosphinico prostaglandin ~~derivative~~ compound having a structure selected from the group consisting of:



wherein bond a is selected from the group consisting of a single bond, a *trans* double bond, and a triple bond;

each of bonds b, c, d, e, and f are independently selected from the group consisting of a single bond and a double bond;

each of bonds g, h, i, and j are independently selected from the group consisting of nil, a single bond, and a double bond;

bond k is selected from the group consisting of a single bond and a double bond;

R^1 is selected from the group consisting of a hydrogen atom, a monovalent hydrocarbon group having 1 to 4 carbon atoms, and a monovalent heterogenous group having 1 to 4 member atoms;

R^2 is selected from the group consisting of a hydrogen atom, a monovalent hydrocarbon group, a substituted monovalent hydrocarbon group, a monovalent heterogeneous group, a substituted monovalent heterogeneous group, a carbocyclic group, a substituted carbocyclic group, a heterocyclic group, a substituted heterocyclic group, an aromatic group, a substituted aromatic group, a heteroaromatic group, and a substituted heteroaromatic group;

R^3 is selected from the group consisting of an oxygen atom, a sulfur atom, and NH;

R^4 is selected from the group consisting of an oxygen atom and a sulfur atom;

R^5 is a divalent group selected from the group consisting of a hydrocarbon group, a substituted hydrocarbon group, a heterogeneous group, and a substituted heterogeneous group;

R^6 is nil or a divalent group selected from the group consisting of $-CH_2-$, -C(O)- and $-C(R^{10})(OR^{10})-$;

R^7 is nil or a divalent group having the formula $-(CD(D))_p-X-(CD(D))_q-$, wherein p is an integer from 0 to 3 and q is an integer from 0 to 3, X is selected from the group consisting of an oxygen atom, a divalent hydrocarbon group, a sulfur atom, SO, SO_2, and ND, and each D is independently selected from the group consisting of a hydrogen atom, a monovalent

hydrocarbon group of 1 to 4 carbon atoms, and a monovalent heterogenous group of 1 to 4 member atoms;

R^8 is selected from the group consisting of a hydrocarbon group, a substituted hydrocarbon group, a heterogenous group, a substituted heterogenous group, a carbocyclic group, a substituted carbocyclic group, a heterocyclic group, a substituted heterocyclic group, an aromatic group, a substituted aromatic group, a heteroaromatic group, and a substituted heteroaromatic group;

R^9 is selected from the group consisting of a hydrogen atom, a monovalent hydrocarbon group of 1 to 4 carbon atoms, and a monovalent heterogenous group of 1 to 4 member atoms;

R^{10} is selected from the group consisting of a hydrogen atom, a monovalent hydrocarbon group of 1 to 4 carbon atoms, and a monovalent heterogenous group of 1 to 4 member atoms;

M^1, M^2, M^3, and M^4 are each independently selected from the group consisting of a carbon atom and a heteroatom, with the proviso that no two heteroatoms may be adjacent;

R^{11}, R^{12}, R^{13}, and R^{15} are each independently selected from the group consisting of nil, a halogen atom, a heteroatom, and R^2, with the provisos that

optionally, R^{11} and R^{12}, R^{12} and R^{13}, or R^{11} and R^{13} may be bonded together to form a ring structure such as a carbocyclic group, a heterocyclic group, an aromatic group, a heteroaromatic group, a substituted carbocyclic group, a substituted heterocyclic group, a substituted aromatic group, or a substituted heteroaromatic group,

when R^{11} is OR^9, R^{12} is a hydrogen atom, and M^2 is a carbon atom; R^{13} is not a hydrogen atom, OR^9, a monovalent hydrocarbon group of 1 to 4 carbon atoms, a monovalent heterogenous group of 1 to 4 carbon atoms, a substituted monovalent hydrocarbon group of 1 to 4 carbon atoms, or a substituted monovalent heterogenous group of 1 to 4 carbon atoms,

R^{13} is not $N(R^9)(OR^9)$ when bond g is a single bond and R^{13} is not NOR^9 when bond g is a double bond, and

R^{13} is not OR^9 when R^{11} is OR^9; M^1, M^2, M^3, and M^4 are each carbon atoms, and R^{12} is a hydrogen atom;

R^{16} is selected from the group consisting of $-CH_2-$, -NH-, and $-NR^{19}-$, wherein R^{19} is selected from the group consisting of hydrocarbon groups, substituted hydrocarbon groups, heterogenous groups, and substituted heterogenous groups; with the proviso that R^{19} may optionally be bonded together with R^8 to form a ring structure selected from the group consisting of heterocyclic groups and substituted heterocyclic groups;

R^{17} is selected from the group consisting of $-SO_2-$, C(O)-, and $-CH_2-$;

R^{18} is selected from the group consisting of a sulfur atom and $-CH_2-$; and

an optical isomer of the structure described above, a diastereomer of the structure, an enantiomer of the structure, a pharmaceutically-acceptable salt of the structure, a

biohydrolyzable amide of the structure, a biohydrolyzable ester of the structure, and a biohydrolyzable imide of the structure.

2. The ~~derivative~~ compound of claim 1, wherein R^1 is selected from the group consisting of a hydrogen atom and a monovalent hydrocarbon group.

3. The ~~derivative~~ compound of claim 2, wherein R^1 is a monovalent hydrocarbon group having 1 to 3 carbon atoms.

4. The ~~derivative~~ compound of claim 3, wherein R^1 has 1 to 2 carbon atoms.

5. The ~~derivative~~ compound of claim 4, wherein R^1 has 1 carbon atom.

6. The ~~derivative~~ compound of claim 2, wherein R^1 is a hydrogen atom.

7. The ~~derivative~~ compound of claim 1, wherein R^2 is a hydrogen atom.

8. The ~~derivative~~ compound of claim 1, wherein R^3 is an oxygen atom.

9. The ~~derivative~~ compound of claim 1, wherein R^4 is an oxygen atom.

10. The ~~derivative~~ compound of claim 1, wherein R^5 is a hydrocarbon group having 1 to 5 carbon atoms in its chain.

11. The ~~derivative~~ compound of claim 10, wherein R^5 has a *cis* double bond at position C_5-C_6 position.

12. The ~~derivative~~ compound of claim 1, wherein R^6 is $-C(R^{10})(OR^{10})-$.

13. The ~~derivative~~ compound of claim 1, wherein R^7 is selected from the group consisting of $-CH_2O-$, $-CH=CH-$, $-CH=C=CH-$, $-CH_2S-$, $-CH_2CH_2-$, $-CH_2NH-$, $-CH_2NCH_2-$, and $-CH_2O(CH_2)_3O-$.

14. The ~~derivative~~ compound of claim 1, wherein R^8 is selected from the group consisting of a methyl group, aromatic groups, substituted aromatic groups, heteroaromatic groups, and substituted heteroaromatic groups.

15. The compound ~~derivative~~ of claim 1, wherein R^{10} is selected from the group consisting of a hydrogen atom and a monovalent hydrocarbon group of 1 to 4 carbon atoms.

16. The compound ~~derivative of~~ claim 1, wherein bond a is selected from the group consisting of a single bond and a *cis* double bond

17. The compound ~~derivative of~~ claim 1, wherein 0 to 1 of bonds b, c, d, e, and f is a double bond.

18. The compound ~~derivative of~~ claim 1, wherein bond h is a single bond.

19. The compound ~~derivative of~~ claim 1, wherein bond k is a single bond.

20. The compound ~~derivative of~~ claim 19, wherein one of M^1, M^2, M^3, and M^4 is a heteroatom.

21. The compound ~~derivative of~~ claim 19, wherein M^1, M^2, M^3, and M^4 are each carbon atoms.

22. The compound ~~derivative of~~ claim 1, wherein R^{12} is a hydrogen atom.

23. The compound ~~derivative of~~ claim 1, wherein R^{11} is selected from the group consisting of a hydrogen atom, an oxygen atom, and OR^9.

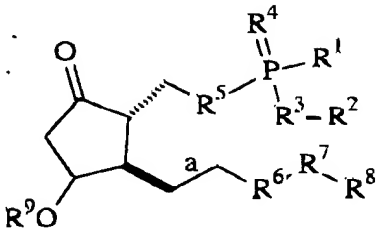
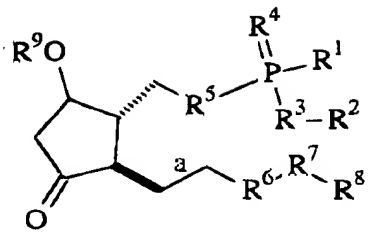
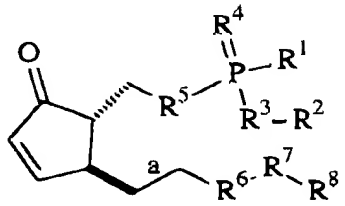
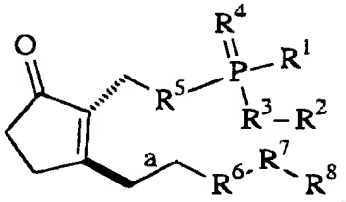
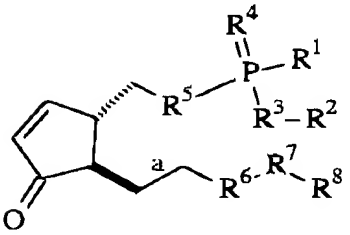
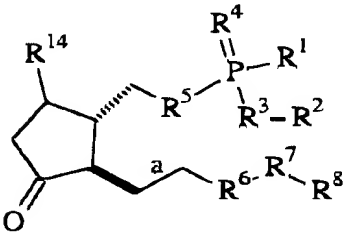
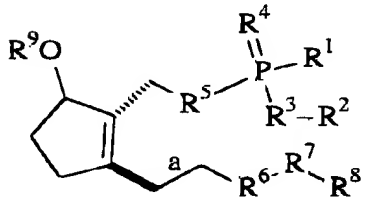
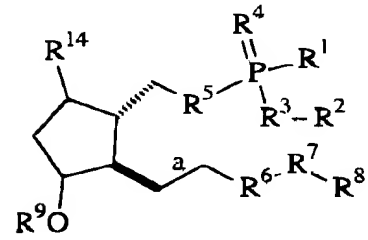
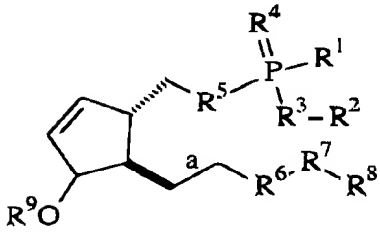
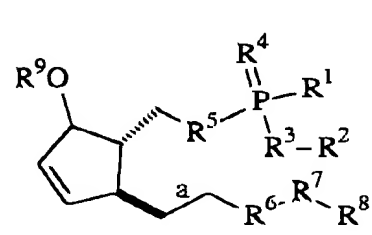
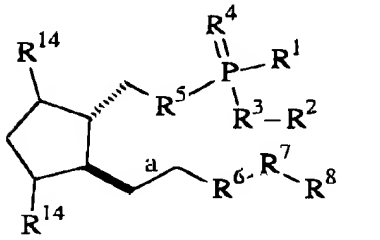
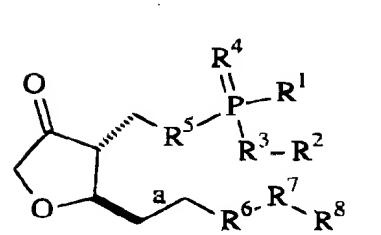
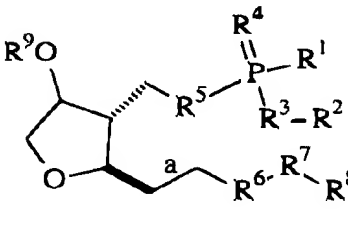
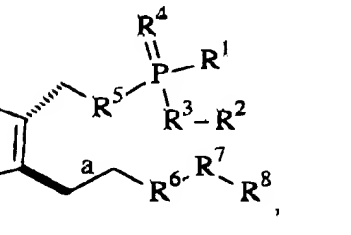
24. The compound ~~derivative of~~ claim 1, wherein R^{13} is selected from the group consisting of a hydrogen atom, an oxygen atom, and OR^9.

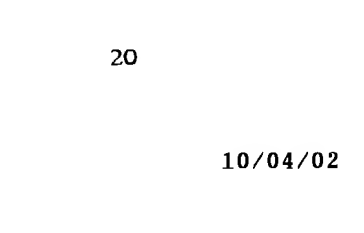
25. The compound ~~derivative of~~ claim 1, wherein R^{16} is $-CH_2-$.

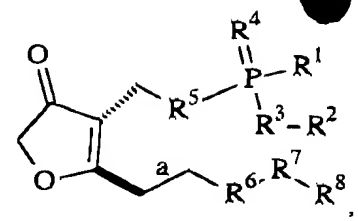
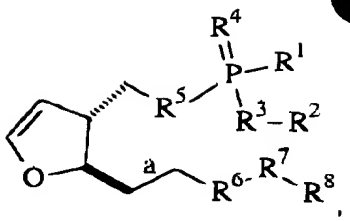
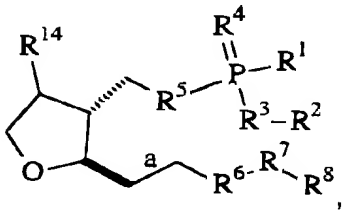
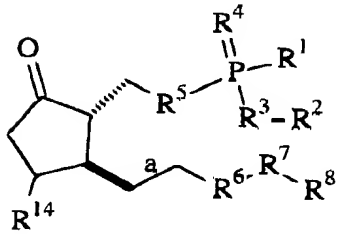
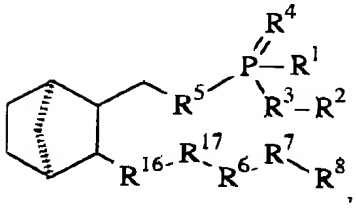
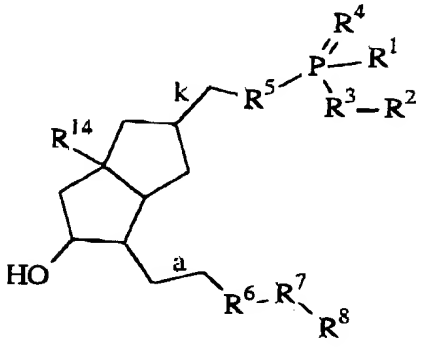
26. The compound ~~derivative of~~ claim 1, wherein R^{17} is $-CH_2-$.

27. The compound ~~derivative of~~ claim 1, wherein R^{18} is $-CH_2-$.

28. The compound ~~derivative of~~ claim 1, wherein the derivative has a structure selected from the group consisting of:

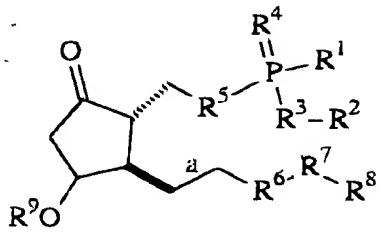
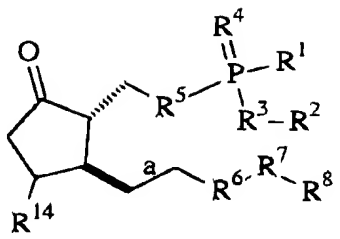
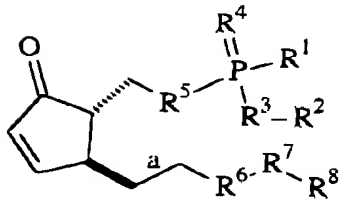
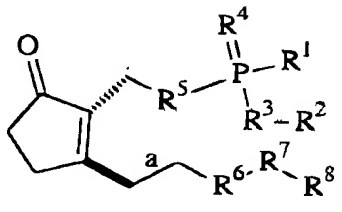
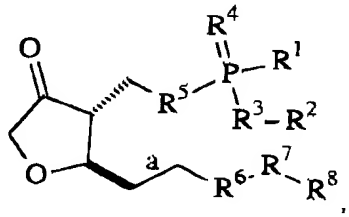
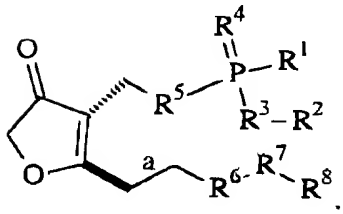

















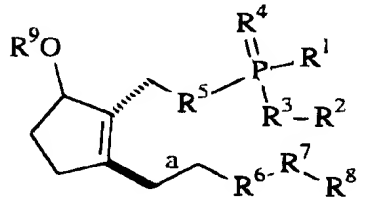
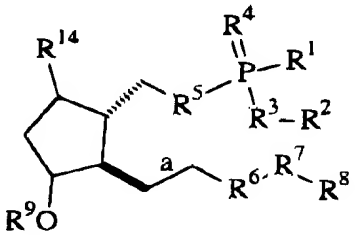
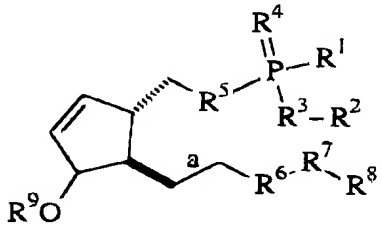
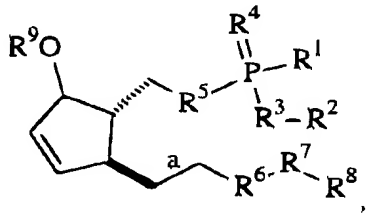







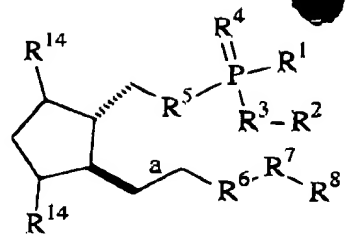
wherein R^{14} is independently selected from the group consisting of nil, a hydrogen atom, a halogen atom, a monovalent hydrocarbon group of 1 to 4 carbon atoms, and a monovalent heterogenous group of 1 to 4 member atoms.

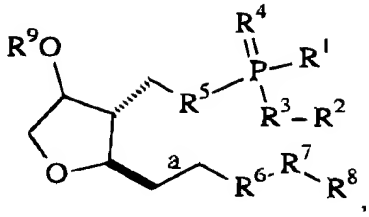
29. The compound ~~derivative of~~ claim 28, wherein the derivative is a prostaglandin E derivative having a structure selected from the group consisting of:

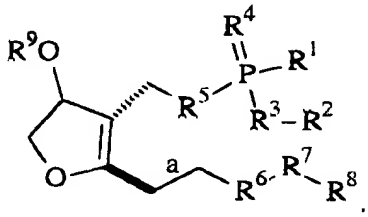





and


30. The compound ~~derivative~~ of claim 28, wherein the derivative is a prostaglandin F derivative having a structure selected from the group consisting of:

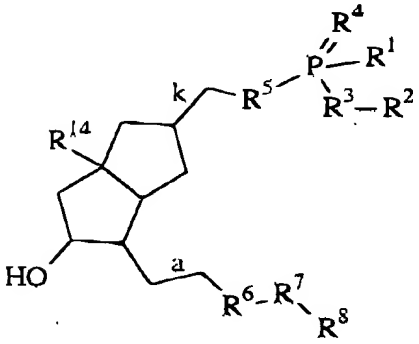







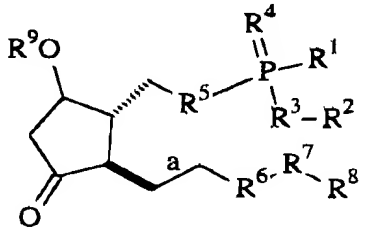


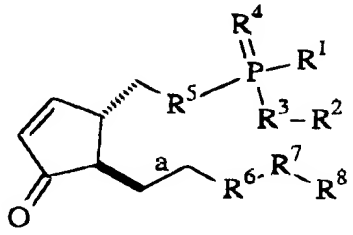


31. The compound ~~derivative~~ of claim 28, wherein the derivative is a prostaglandin I derivative having the structure:

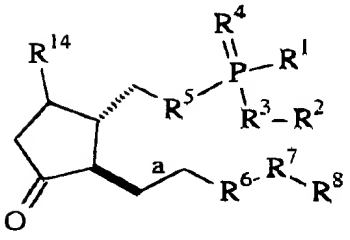


32. The compound ~~derivative~~ of claim 28, wherein the derivative is a prostaglandin D derivative selected from the group consisting of:





and



33. The compound ~~derivative~~ of claim 28, wherein the derivative is a thromboxane having the structure: